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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademark

Office Action Summary	Application No. 09/402,260	Applicant(s) Kawashima et al.
	Examiner CB Wilder	Group Art Unit 1655

☒ Responsive to communication(s) filed on *Sep 30, 1999* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-17, 21, and 23* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-17, 21, and 23* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Priority

1. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/402,260, filed on September 30, 1999.

Claim Objections

2. Claims 1-17 are objected to because of the following informalities:

(a) Claims 1-17 are objected to because the word "hybridised" in claims 1 (a) and (b), 15 and 17 (a) and (b) is misspelled. It is suggested changing "hybridised" to "hybridized".

(b) In claims 6, the word "immobilised" is misspelled. It is suggested changing "immobilised" to "immobilized". Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-17, 21 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-17 lacks proper antecedent basis in claim 1 (c) and claim 17 (c) for " the appropriate position" because the prior steps to not recite a position. It is suggested changing "the" to "a".

(b) Claim 1-17 are indefinite for being incomplete because claim 1 is drawn to a method for sequencing but lacks a step in which nucleic acid molecules are sequenced. It is also unclear how claim 1 operates with one nucleotide "sequences" a nucleic acid.

(c) Claim 2 is *non sequitur* to claim 1 or any other claim because it has no recited relationship to the claimed method.

(d) Claim 4 is indefinite in the recitation of "e.g." (meaning "for example") because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

(e) Claims 7-9 are confusing at the recitation of a "use" for the method because it is unclear if the recited "10 or more, "100 or more" or 1000 or more" nucleic acid molecules are sequenced. Clarification is required.

(f) Claims 21 and 23 are confusing at "by incorporated" in step (c) because of improper grammar. It is suggested changing "incorporated" to "incorporation".

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the

subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-18 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rabani (WO 96/27025 September 1996) in view of Brenner (5,863,722 effective filing date October 1994). Regarding claims 1 and 2, Rabani discloses a method for sequencing nucleic acid molecules, comprising providing a population (plurality) of single molecules at a first location and at a second location, a distinct second sequence of a sample (page 41, lines 35-40 and page 42, line 1-3), wherein the nucleic acid molecules are hybridized to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase; providing each location with a nucleic acid polymerase and a given labeled nucleotide type under conditions that allow extension on the primers if a complementary base or a plurality of such bases is present at the appropriate position (page 42, lines 14-23); detecting whether or not the labeled nucleotide has been used for primer extension at each location by determining whether or not the label is present on said nucleotide has been incorporated into extended primers; and repeating the steps one or more times so that extended primers comprising a plurality of labels are provided (Page 42, lines 23-41 and page 43, lines 1-7) to obtain all or part of a sequence that is converted to provided a complementary sequence thereto (age page 43, lines 10-15). Rabani additionally teaches that the method is advantageous for sequencing diverse populations of single molecules but does not tech sequencing diverse populations of identical molecules (page 7, lines 38-41). In a method similar to that of Rabani, Brenner teaches sequencing nucleic acid molecules comprising providing populations of identical single-stranded nucleic acid

molecules (having the same sequence as one another) that are analyzed simultaneously by primer extension via automated molecular systems (column 3, lines 25-44, 66-67 and column 4, lines 4-6) (*See also column 20, line 47-column 21, line 12 for "Automated System"*). It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Rabani with the teachings of Brenner to obtain the claimed invention because the skilled artisan would have been motivated to sequence diverse populations of identical nucleic acid molecules with a reasonable expectation of success for the benefit of increasing large-scale DNA sequencing and lowering of sequencing cost in a significant manner as taught by Brenner (column 2, lines 12-15 and column 4, lines 2-6).

Claim 3 is drawn to an embodiment of claim 1, wherein if the given nucleotide has been used in primer extension in step (d) then this step includes the step of detecting how many of the given nucleotides have been used per extended primer. Rabani suggest this embodiment (page 42, lines 15-25).

Claim 4 is drawn to an embodiment of claim 1, wherein after step (c) excess nucleotides that have been used in primer extension are removed. Rabani discloses wherein excess nucleotides that have been used in primer extension are removed by washing (page 42, lines 23-25).

Claim 5 is drawn to an embodiment of claim 1, wherein step (d) uses absorption or emission spectrometry. Rabani discloses this embodiment (page 44, lines 3-15 and lines 28-33).

Claim 6 is drawn to an embodiment of claim 1, wherein said single-stranded nucleic acid molecules, said primers or both of the aforesaid are immobilized (page 42, lines 3-5).

Claims 7-9 are drawn to an embodiment of claim 1 wherein the method is used to fully or partially sequence 10 or more (claim 7), 100 or more (claim 8), or 1000 or more (claim 9) nucleic acid molecules having different sequences simultaneously. Rabani disclose that the method is used to sequence information relative to the total complexity of an initial DNA sample and that data is recorded to reconstruct sequence information for a segment of each sample template molecule (page 43, lines 10-14). Rabani implies the claimed embodiments.

Claim 10 and 11 are drawn to an embodiment of claim 1, wherein each of the four different nucleotides is used in primer extension (claim 10) and the four different nucleotides are used in a predetermined order in repeated cycles. Rabani discloses this embodiment (page 42, lines 16-17 and page 43, lines 2-7).

Claims 12 and 13 are drawn to an embodiment of claim 10 wherein the nucleotides are dATP, dTTP, dGTP and dCTP in labeled form or wherein the nucleotides are ATP, UTP, GTP and CTP in labeled form. Rabani discloses wherein each of four different nucleotides is used in primer extension and is labeled form (page 42, lines 16-25). Rabani does not expressly teach wherein the nucleotides are dATP, dTTP, dGTP and dCTP or ATP, UTP, GTP and CTP. However, it is well known in the prior art that dATP, dTTP, dGTP and dCTP or ATP, UTP, GTP and CTP are used in labeled form in a number of methods involving primer extension in DNA or RNA samples.

Claim 14 is drawn to an embodiment of claim 1, wherein the detection step is carried out without moving the nucleic acid molecules from the different locations. Rabani discloses this embodiment (page 42, lines 32-35 and page 43, lines 23-33).

Claim 15 is drawn to an embodiment of claim 1 with the exception that double stranded nucleic acid molecules having nicks therein are provided at the first and/or second locations instead of providing single-stranded molecules hybridized to primers. Rabani disclose this embodiment (page 48, lines 13-26).

Claim 16 is drawn to an embodiment of claim 1 except that only one nucleic acid molecule is provided at the first and or second locations. Rabani discloses wherein only one nucleotide type is provided at each location (page 42, lines 20-22).

The order of combination of method steps as described in claims 17 and 21 is not critical to the claimed invention. *In re Burhans*, 69 USPQ 330 states that a selection of any order of performing process steps is **prima facie** obvious in the absent of new or unexpected results.

Claim 18 is an apparatus for performing a method according to claim 1, the apparatus comprising a plurality of nucleotides, a nucleic acid polymerase and detection means. Rabani discloses a device (page 43, lines 16-35, page 12, line 37) for performing a sequencing method which uses a plurality of nucleotides (page 42, lines 18-23), a nucleic acid polymerase (page 42, line 20). and which device comprises detection means. The device means are suitable for distinguishing between different locations (page 13, lines 13-32).

Claim 23 is drawn to an embodiment of claim 21 with the exception that instead of hybridizing a target nucleic acid molecule to a primer and extending the primer with labeled nucleotides, a nick is introduced into a double stranded nucleic acid molecule and the nick is extended using nick translation and labeled nucleotides. Rabani discloses this embodiment (page 48, lines 13-24).

Conclusion

7. No claims are allowed

8. Any inquiry concerning this communication or earlier communications from the Exr. should be directed to Exr. Cynthia Wilder whose telephone number is (703) 305-1680. The Exr. can normally be reached on Monday through Thursday from 7:00 am to 5:00 pm.

If attempts to reach the Exr. by telephone are unsuccessful, the Exr.'s supervisor, W. Gary Jones, can be reached at (703) 308-1152. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed the Group's receptionist whose telephone number is (703) 308-0196.

Cynthia B. Wilder, Ph.D.

May 16, 2000

STEPHEN G. WALKER
PRIMARY EXAMINER